Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Note

REG2000-15

Azoxystrobin

The active ingredient azoxystrobin and the formulated products Quadris Flowable Fungicide, Quadris Fungicide, Abound Flowable Fungicide, Abound Fungicide and Heritage Fungicide containing azoxystrobin for the control of various plant diseases of canola, grapes and turf in Canada, have been granted Section 17 temporary registrations.

This regulatory note provides a summary of data reviewed and the rationale for the regulatory decision concerning these products.

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Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) has issued temporary registrations for Quadris Flowable Fungicide, Quadris Fungicide, Abound Flowable Fungicide, Abound Fungicide and Heritage Fungicide developed by Zeneca Agro for use in canola, grapes and turf.

Methods for analyzing azoxystrobin residues in environmental media are available to research and monitoring agencies upon request to the PMRA.

Zeneca Agro will be carrying out additional residue, environmental and efficacy studies as a condition of this temporary registration. Following the review of this new data, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

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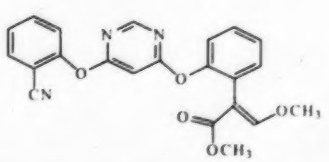
1.0 The active substance, its properties, uses, proposed classification and labelling

1.1 Details of the proposed uses

Azoxystrobin is a broad spectrum fungicide from the strobilurin group of compounds. It exerts its fungicidal activity by inhibiting mitochondrial respiration in fungi. Azoxystrobin is a systemic compound that is translocated in the transpiration stream from the roots to the stem and into the leaves. Taken up by leaves, roots and seeds, it is claimed to have protectant and eradicant properties. Compared with the major classes of systemic fungicides, azoxystrobin has a high level of intrinsic activity and the broadest spectrum; therefore, it is active at very low doses against a wide range of fungal pathogens.

Azoxystrobin is registered as a foliar-applied fungicide on numerous crops in Europe and the United States. It was proposed for Canadian registration on grapes, canola and turf to control various disease. See Appendix I for more details on the accepted uses.

1.2 Identity of the active substance and preparations containing it

Active substance:	Azoxystrobin
Function:	Fungicide
Chemical name:	
1. International Union of Pure and Applied Chemistry:	methyl (*E*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy] phenyl}-3-methoxyacrylate
2. Chemical Abstract Services (CAS):	methyl (*E*)-2-[[6-(2-cyanophenoxy)-4-pyrimidinyl] oxy]-α-(methoxymethylene)benzeneacetate
CAS number:	131860-33-8
Nominal purity of active:	96% (nominal)
Identity of relevant impurities of toxicological, environmental or other significance:	The technical grade azoxystrobin does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track-1 substances.
Molecular formula:	$C_{22}H_{17}N_3O_5$
Molecular mass:	403.4
Structural formula:	

1.3 Physical and chemical properties of the active substance

Azoxystrobin: pure material, except as marked technical grade active ingredient (TGAI)

Property	Result	Comment
Colour, odour and physical state	White powder with no characteristic odour	
Melting point or range	116°C	
Density (TGAI)	1.25 g/mL	
Vapour pressure	1.1×10^{-13} kPa	Relatively nonvolatile under field conditions
UV and visible spectrum	λ_{max} (nm) / ϵ ($mol^{-1}cm^{-1}$): 202 / 60700; 242 / 17800; 295 / 302	Low potential for ultraviolet phototransformation under normal environmental conditions
Solubility in water at 20°C (mg/L)	6	Low solubility in water
Solubility in organic solvents at 20°C, 96.2% pure material	Solvent / Solubility (g/L): *n*-hexane 0.57; octan-1-ol 1.4; methanol 20; toluene 55; acetone 86; ethyl acetate 130; dichloromethane 400	
n-Octanol–water partition coefficient (K_{ow}) at 20°C	log K_{ow}: 0.39 / K_{ow}: 2.5	Unlikely to bioconcentrate or bioaccumulate
Dissociation constant (pK_a)	None found (not expected to dissociate)	
Oxidizing properties (TGAI)	Not an oxidizer	

End-use product (formulation)

	Quadris Fungicide Abound Fungicide	Heritage Fungicide	Quadris Flowable Fungicide Abound Flowable Fungicide
Physical state	Solid, free flowing granules	Solid, free flowing granules	Uniform, opaque, viscous liquid
Formulation type	Wettable granule	Wettable granule	Suspension concentrate
Guarantee	800 g/kg azoxystrobin (nominal)	500 g/kg azoxystrobin (nominal)	250 g/L azoxystrobin (nominal)
pH of a 1% dispersion in water	10.39	7.14	7.64

1.4 Classification and labelling

1.4.1 Technical azoxystrobin

Toxicological data: Technical azoxystrobin is of low acute toxicity by the oral and dermal routes of exposure and slightly toxic by the inhalation route of exposure. It is a minimal eye and dermal irritant and not a dermal sensitizer.

1.4.2 Quadris Flowable Fungicide (250 g/L) and ABOUND Flowable Fungicide (250 g/L)

Toxicological data: The formulation is of low acute toxicity by the oral, dermal and inhalation routes of exposure. It is a mild eye irritant and a minimal dermal irritant and not a dermal sensitizer.

1.4.3 Quadris Fungicide (800 g/kg) and ABOUND Fungicide (800 g/kg)

Toxicological data: The formulations are of low acute toxicity by the oral, dermal and inhalation routes of exposure. They are mild eye irritants, minimal dermal irritants and not dermal sensitizers.

1.4.4 Heritage Fungicide (500 g/kg)

Toxicological data: The formulation is of low acute toxicity by the oral, dermal and inhalation routes of exposure. It is a mild eye irritant, a slight dermal irritant and not a dermal sensitizer.

2.0 Methods of analysis

2.1 Methods for analysis of the active substance as manufactured

The active substance and significant related impurities (content ≥ 0.1%) in the technical product were determined by validated specific methods using gas chromatography (GC).

2.2 Method for formulation analysis

A capillary GC method with flame ionization detection was used for the determination of active substance in each of the end use products. The method has been shown to have satisfactory specificity, linearity, precision and accuracy.

2.3 Methods for residue analysis (see Appendix II)

2.3.1 Multi-residue methods for residue analysis

Azoxystrobin could not be quantified by accepted multi-residue methods.

2.3.2 Methods for residue analysis of plants and plant products

The residue of concern (ROC) was defined from the plant metabolism studies as methyl (*E*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate including the isomer methyl (*Z*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate.

Two methods were submitted for analysis of residues in food and feed matrices. The methods were able to resolve both the parent and the *Z*-isomer with a limit of quantitation (LOQ) of 0.01 ppm for each. The chromatograms submitted in support of these methods (nitrogen–phosphorus detection [NPD]–GC) were free of matrix interference in the areas of analyte elution. These methods were validated in the range of expected residues for accuracy and precision. The recoveries obtained from a large number of spiked samples were acceptable. These methods were successfully validated by an independent laboratory.

2.3.3 Methods for residue analysis of food of animal origin

A single method for analysis of residues in animal matrices was submitted. The method was able to resolve both the parent and the *Z*-isomer with an LOQ of 0.01 ppm for each in all matrices, with the exception of milk where the LOQ was 0.006 ppm for both isomers. The chromatograms submitted in support of these methods (NPD–GC) were free of matrix interference in the areas of analyte elution. These methods were validated in the range of expected residues for accuracy and precision. The recoveries obtained from spiked samples were acceptable.

3.0 Impact on human and animal health

3.1 Integrated toxicological summary (see also Toxicology summary table, Appendix III)

Azoxystrobin administered orally to rats was rapidly and extensively absorbed and distributed into all tissues. Elimination was rapid and mainly in the feces (via the bile) with no evidence of accumulation in tissues. Excretion via expired air was minimal. Repeated oral administration did not alter either the absorption or the excretion pattern. Sex-related differences in excretion and metabolism were minor, although excretion in the urine was slightly higher in females. Biliary metabolites accounted for the greatest amount of absorbed dose in both sexes, mainly at the methoxyacid on the phenylacrylate moiety by hydroxylation and conjugation with glucuronide and, secondly, at the cyanophenyl moiety by hydroxylation and conjugation with glucuronide, glutathione, cysteine, cysteinyl–glycine or mercapturate. Minor amounts of ester cleavage and demethoxylation of the phenylacrylate moiety were observed. No parent compound was detected in the bile or urine. Supplemental plasma absorption studies in nonpregnant and pregnant rabbits showed a similar pattern of rapid absorption and elimination with the methoxyacid metabolite prominent in the plasma and at much higher concentrations than the parent compound.

In laboratory animals, azoxystrobin was of low acute toxicity via the oral and dermal routes of exposure and slightly acutely toxic via the inhalation route of exposure. It was minimally irritating to the eye and skin and not a dermal sensitizer.

In subchronic repeat dosing studies in mice, rats and dogs, the toxicity of azoxystrobin was of a similar order of magnitude following oral administration. The subchronic no observable effect levels (NOEL) for systemic toxicity were 17 mg/kg body weight (bw) per day in mice (90-day) and 20 mg/kg bw/day in rats (90-day), and the overall no observable adverse effect level (NOAEL) was 25 mg/kg bw/day (1-year) in dogs. No evidence of toxicity was observed in rats following dermal exposure at a limit dose of 1000 mg/kg bw/day. Toxicity was cumulative in the rat where longer term exposures produced an increased incidence and severity of pathology at lower effect levels. The chronic NOELs for systemic toxicity were 18 mg/kg bw/day in rats (2-year dietary) and 38 mg/kg bw/day in mice (2-year dietary).

The most common indicators of toxicity were reduced body weight gain, increased liver weight and altered clinical chemistry parameters indicative of an effect on the liver. The principal target organs were the bile duct (rats) and liver (mice, rats, dogs). In rats, increased liver weights and altered clinical chemistry parameters (liver) were observed in males and females with pathology of the bile duct and liver observed in males as cholangitis of the extrahepatic bile duct with proliferation of the intrahepatic bile ducts or ductules and oval cells and either hepatocellular hyperplasia or hepatitis. In dogs, although liver pathology was not observed at the dose levels tested, evidence of an effect on the liver was suggested by the presence of increased liver weights and altered clinical chemistry parameters. In mice, increased liver weight and liver pathology (periportal

eosinophilia) were observed in both males and females. Chronic exposure in rats included distension of the common bile duct and marked biliary hyperplasia in the liver. The observed liver and biliary lesions in the rat correlate with the observed high degree of metabolism and biliary elimination. The rat was identified as the most sensitive species in demonstrating liver toxicity.

Gender sensitivity was evident in rats where the male was more sensitive, demonstrating clear pathology of the common bile duct and liver following subchronic and chronic dietary exposures and reduced survival following chronic dietary administration. In females, at similar dose levels, subchronic and chronic exposure did not produce bile duct or liver pathology. although an effect was suggested by increased liver weight and altered clinical chemistry parameters and confirmed in the published literature, which described a 28-day dose range-finding dietary study in rats where pathology of the bile duct and liver was observed in females at much higher doses.

Azoxystrobin was not oncogenic in rats and mice. Genotoxicity studies indicate that azoxystrobin is not mutagenic in vivo in mammals.

Azoxystrobin was not a reproductive toxicant. A NOEL for reproductive toxicity was 34 mg/kg bw/day based on reduced pup body weight and increased liver weight in F_1 and F_2 litters at the next higher dose level (175 mg/kg bw/day). A NOEL for parental systemic toxicity was 32 and 34 mg/kg bw/day for males and females, respectively, based on reduced body weight and food consumption, increased liver weight and pathology of the liver and bile duct in males at the next higher dose level (165 and 175 mg/kg bw/day in males and females, respectively). No evidence of age-related sensitivity was observed where effects on the offspring of rats and rabbits occurred only at or above maternally toxic doses. In the reproductive toxicity study in the rat, the incidence of bile duct and liver pathology was increased in F_1 males compared with F_0 males; however, the difference was attributed to an increased duration of exposure.

No teratogenic effects were observed in either rats or rabbits exposed to azoxystrobin via oral gavage. The NOAEL for maternal toxicity was 25 and 150 mg/kg bw/day for rats and rabbits, respectively, based on observed clinical signs and reduced body weight and food consumption. The NOAEL for developmental toxicity in rats was 100 mg/kg bw/day based on a marginal delayed ossification of metatarsals. The NOEL for developmental toxicity in rabbits was 500 mg/kg bw/day (highest dose) in the absence of any observed effects.

Azoxystrobin was not selectively neurotoxic following acute gavage or subchronic dietary administration in rats. The acute NOEL for neurotoxicity is 2000 mg/kg bw/day and the subchronic NOEL for neurotoxicity is 161 mg/kg bw/day. No clinical signs, neurobehavioral effects or pathology of neurological tissues were observed at an acute limit dose of 2000 mg/kg bw or following subchronic dietary administration up to 161 or 202 mg/kg bw/day in males and females, respectively.

3.2 Allowable daily intake

The recommended allowable daily intake (ADI) for azoxystrobin is 0.18 mg/kg bw/day. The most appropriate study for selection of a toxicity end point for chronic dietary exposure was the 2-year dietary study in rats, with a NOEL of 18 mg/kg bw/day in males where reduced survival and growth and marked bile duct and liver pathology was observed at and above 34 mg/kg bw/day. The rat was considered the most sensitive species for demonstrating target organ toxicity following subchronic and chronic dietary administration, with evidence of gender sensitivity and cumulative toxicity in males. By applying a 100-fold safety factor to the NOEL (10-fold each for intraspecies and interspecies differences), an ADI of 0.18 mg/kg bw/day was determined.

3.3 Acute reference dose

An acute reference dose is not required for azoxystrobin, which is of low acute toxicity by the oral route of exposure. No specific neurotoxicity was observed in the acute neurotoxicity study in rats, and observed clinical signs in the dog and rat in repeat gavage or capsule studies were attributed to bolus gavage dosing or gastric irritation, or they occurred only at dose levels producing systemic toxicity. No clinical signs of acute toxicity were observed in any of the dietary studies.

3.4 Toxicology end point selection

Complete and acceptable toxicology data were available for review of the new technical active ingredient, azoxystrobin.

For the defined exposure scenarios, the subchronic dermal toxicity study (21-day) in rats was considered the most relevant study for toxicity end point selection (NOEL = 1000 mg/kg bw/day) based on the following considerations:

- The study most closely represents the anticipated exposure pattern in humans (short-term to intermediate duration, dermal route of exposure). Although a longer duration toxicity study may better reflect the exposure duration, a dermal study was considered most relevant, given the predominantly dermal route of exposure that accounted for greater than 97% of the potential exposure.

- Azoxystrobin was of low acute toxicity in rats via the dermal route of exposure and no significant systemic toxicity was observed at a limit dose of 2000 mg/kg bw. In a short-term (21-day) dermal toxicity study in rats, no evidence of toxicity was observed at the limit dose of 1000 mg/kg bw/day where a full range of parameters were investigated including clinical signs, body weight gain, hematology, clinical chemistry and macroscopic and microscopic pathology.

- Azoxystrobin has been shown to be rapidly and extensively metabolized and excreted in the rat with no evidence of bioaccumulation following repeat oral exposures. Significantly less absorption (10-fold) occurred following dermal vs. oral routes of administration.

- The dose–response curve for azoxystrobin toxicity has been well characterized in several species (mouse, rat, dog) following subchronic and chronic oral administration. Subchronic oral exposure in all species produced a similar range of effects at comparative effect levels. Chronic toxicity studies showed qualitatively similar toxicity and target organ as in the subchronic toxicity studies and at similar effect levels, although toxicity was cumulative in the male rat following chronic exposure with lower effect levels. Azoxystrobin was not tumorigenic in rats or mice, was not mutagenic or clastogenic in vivo, was not teratogenic in rats or rabbits and was not considered a reproductive toxicant or a neurotoxicant.

- A margin of exposure (MOE) of 100 is recommended to account for intraspecies and interspecies differences. An additional safety factor for age-related susceptibility is not warranted.

3.5 Impact on human health arising from exposure to azoxystrobin

3.5.1 Operator exposure assessment

Farmers could treat approximately 115 ha of canola and 15 ha of grapes in a day. Canola could also be treated by custom applicators, who could treat approximately 315 ha/day. Aerial application to canola could result in 400 ha being treated in a day. Approximately 8 ha of turf at either golf courses or sod farms could be treated in a day with groundboom equipment. For spot treatment of turf using a hand wand, less than 1 ha would be treated in a day. At the maximum application rates, approximately 29 kg active ingredient (a.i.) per day and 79 kg a.i./day could be mixed, loaded and applied by groundboom to canola by farmers and custom applicators, respectively. During aerial application, 100 kg a.i./day could be handled. Airblast application to grapes could result in 4 kg a.i. being handled per day and 10 kg a.i. could be handled per day for turf applications by groundboom. Application of azoxystrobin would be intermittent and could occur from late spring to early fall, depending on the site and disease being treated. Therefore, as a worst case, some workers (e.g., custom applicators) could be exposed for up to several weeks, intermittently over the growing season.

In a dermal absorption study, 24 male rats were administered 40 μL of ICIA5504 ([^{14}C]-pyrimidinyl ICIA5504 and unlabeled ICIA5504) to a 10 cm^2 area at doses of 0.001, 0.01, 0.09 or 1.33 mg/cm^2. Dermal absorption was determined at 0.5, 1, 2, 4, 10 and 24 hours. The application site was washed just prior to sacrifice.

No animals died as a result of the treatment. Percutaneous absorption was minimal ($\leq$13.3%) and did not appear to exhibit a dose–response relationship. Limited absorption precluded accurate assessment of distribution and metabolite characterization. Both fecal and urinary excretion were quantified, the former representing 0.6% or less and the latter accounting for less than 0.1% of the absorbed dose over a 24-hour period. Total absorption at 24 hours was 2.9, 13.3, 10.3 and 7.2% for the 1.33, 0.09, 0.01 and 0.001 mg/cm^2 dose groups, respectively. The absorbed dose included the residues found in the urine, feces cage washing, the skin at the application site and the residual carcass.

Unabsorbed dose included the skin wash, non-occlusive covering and the untreated skin. Overall recovery of administered radioactivity was 95–105%.

A Pesticide Handlers Exposure Database (PHED) version 1.1 assessment was designed to assess the mix, load and application exposure during the handling and application of the five end-use azoxystrobin products formulated as either a wettable granular or aqueous suspension and applied by groundboom, air, airblast or hand wand to canola, grapes or turf. The PHED is a database of generic mixer–loader–applicator passive dosimetry data that facilitates the generation of scenario specific exposure estimates. The PHED subsets compare well to the proposed formulations and use-patterns. All PHED subsets except the hand wand application subset meet criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides. The data quality for the hand wand use is of low confidence due to the use of A, B and C grade data and only nine replicates from one study for each body part; therefore, a quantitative estimate of exposure for azoxystrobin during hand wand application to turf could not be generated. The PHED estimates were based on wearing long-sleeved shirts, long pants and gloves when mixing and loading, and long-sleeved shirts, long pants and no gloves when applying. A best-fit statistical measure was used for the exposure estimates.

Exposure estimates are summarised in Appendix V. The highest exposures (dermal deposition) occur during the mixing and loading of Quadris for aerial application to canola (236.43 μg a.i./kg bw/day), and for custom applicators mixing, loading and applying Quadris to canola (225.11 μg a.i./kg bw/day). The exposure is substantially less for the custom applicator and the mixer–loader for aerial application when applying the liquid formulation (ICIA5504 25 SC) to canola as opposed to the dry flowable formulation (Quadris). All other exposure scenarios resulted in less azoxystrobin exposure. Although a quantitative estimate of exposure for the hand wand application of azoxystrobin to turf was not generated, the exposure for mixing, loading and applying azoxystrobin to turf with a hand wand would be much lower than with a groundboom application to turf. This type of application would be spot treatment only, and less than 1 ha would be treated in this manner in a day.

For the risk assessment, the exposure estimates were compared with the 21-day dermal rat study, which had a no observable effect level (NOEL) of 1000 mg/kg bw. The MOEs are summarised in Appendix V.

3.5.2 Bystanders

Given the proposed commercial and agricultural use scenarios, exposure and risk to bystanders should be minimal. Bystander exposure for golfers on treated golf courses would be negligible.

3.5.3 Post-application exposure

Post-application exposure would be minimal for canola as the harvest is mechanical, and any contact with foliage, post-application, would be minimal. There is a potential for post-application exposure to azoxystrobin in grapes and on sod farms. Post-application activities in grape crops that may result in substantial foliar contact include pruning, thinning, tying bunches to the catch wires and harvesting. On sod farms, most of the cutting and rolling of the sod is mechanical; however, the rolled sod is transferred to skids by hand. Further, landscapers generally purchase the sod and lay it within 24–48 hours of it being harvested. Landscapers, therefore, may have some exposure to azxoystrobin via contact with the sod. Post-application exposure could occur for a few weeks; however, after the last application, dislodgeable residue levels of azxoystrobin decline steadily.

A dislodgeable foliar residue (DFR) study was designed to collect data to calculate DFR dissipation curves for azoxystrobin on grape foliage at one test site in California. The application rate (280 g a.i./ha), frequency (six applications) and monitoring times (five sampling times after the final application) were relevant to the use pattern proposed. Although geographical and climatic conditions were not fully representative of Canadian growing regions, the data were considered to be adequate for use in the occupational risk assessment. One site was monitored with four replicates per sampling time per site (total replicates per sampling time was four). A second control site was monitored with two replicates per sampling time per site, with one replicate being used for field fortification.

This study was conducted according to current methodologies. The conditions of study, as well as the relevance to the proposed Canadian use, are consistent with acceptable protocols and guidelines. Although the field recovery data had some inadequacies, the study was considered acceptable.

The results indicate that transferable residues of azoxystrobin increase with multiple applications from 0.39 to 0.65 $\mu g/cm^2$ after the third and sixth applications, respectively. The dissipation rates of the transferable residues after the last (sixth) application followed pseudo first-order kinetics with $R^2 = 0.87$ and a half-life ($t_{½}$) of 17.4 days. For the post-application exposure to grapes, the DFR data was coupled with a generic transfer coefficient of 15 000 cm^2/hour to estimate post-application exposure for workers re-entering grape crops. The DFR results and resulting exposure estimates and margins of exposure are summarised in Appendix V. The highest exposure from re-entry into grape crops would occur following the sixth (last) application, as soon as the residues had dried, and is estimated to be 1 mg/kg bw/day. The resulting MOE based on a NOEL of 1000 mg/kg bw from the 21-day dermal rat study would be 1000.

DFR data was unavailable for post-application activities in sod farms. A generic transfer coefficient of 10 000 cm^2/hour has been developed by the U.S. Environmental Protection Agency (EPA) for sod farm re-entry activities suggesting that the level of foliar contact is higher in grape re-entry activities than commercial sod farm re-entry activities. Due to foliage (i.e., turf vs. grape) and application rate differences (250 g a.i./ha for grapes vs. 600 g a.i./ha for turf) it is not appropriate to use the grape DFR study to derive estimates

of DFR on turf. However, it is likely that the turf applications would result in higher DFR values than the grape applications. It may be possible that workers re-entering turf farms will have higher exposure then those re-entering grape crops. Given the high MOE for re-entry activities with grapes and the decrease in foliar contact with turf, however, it is expected that the MOE for re-entry workers on turf farms would be adequate (i.e., 100 or above).

4.0 Integrated food residue chemistry summary (see Appendix IV)

Metabolism studies submitted demonstrated the fate and disposition of azoxystrobin in grapes, peanuts, wheat, ruminants, poultry and rats. In addition, environmental biotic and abiotic transformations were also considered. Based on the results of these studies, the ROC was defined as the parent plus the *Z*-isomer.

The proposed methods of analysis for azoxystrobin and the *Z*-isomer involved the quantification by means of NPD–GC analysis. The LOQs for the method were set at 0.01 ppm for plant matrices, meat and meat by-products and 0.006 ppm for milk.

The program of supervised field trials conducted in Canada and the U.S. involved the foliar application of azoxystrobin to canola and grapes. The results demonstrated that residues in canola could be as high as 0.8 ppm and that the residues in grapes could be as high as 2.5 ppm. Considering these results, the proposed maximum residue limits (MRL) for azoxystrobin in canola and grape are 1.0 and 2.5 ppm, respectively.

Plant back restrictions have been placed in the proposed labels to ensure that residues of azoxystrobin and the *Z*-isomer in succeeding crops will be below the LOQ of the analytical methods.

Potential exposure to azoxystrobin in the diet is low. On the basis of the Canadian diet, it was estimated that theoretical maximum daily intakes are no more than 12% of the proposed ADI (0.18 mg/kg/day) for any age groups, providing a large safety margin for consumers.

5.0 Fate and behaviour in the environment

5.1 Summary of the fate and behaviour of azoxystrobin in the environment

5.1.1 Transformation (see Appendix VI, Table 1)

Azoxystrobin is stable with respect to hydrolysis at 25°C at pH 5 and 7, and has a $t_{½}$ of 267 days at pH 9. Under normal environmental conditions, hydrolysis is not a major transformation pathway for azoxystrobin.

The phototransformation of azoxystrobin in aqueous solution closely follows first-order kinetics with a $t_{½}$ of 14 Florida summer sunlight days. Azoxystrobin undergoes biphasic phototransformation on soil with a dissipation time 50% (DT_{50}) of 10 Florida summer

sunlight days. The intensity of summer sunlight in Florida is substantially greater than would be found in the Canadian environment and consequently, the rate of photolysis of azoxystrobin at Canadian latitudes is predicted to be slower than the rates reported in these studies. Compounds with a relatively slow rate of phototransformation (more than ~7 days) are likely to be transported to environmental compartments where they are not exposed to direct sunlight (e.g., adsorbed to soil or sediment particles, mixed into deep layers of a water body, etc.). From these results, it is concluded that, under normal environmental conditions, photolysis is a route of transformation for azoxystrobin in soils.

Azoxystrobin biotransforms slowly in soils. Azoxystrobin is moderately persistent in aerobic soils (DT_{50} = 54–135 days) and slightly persistent in anaerobic soils (DT_{50} = 36–45 days). Soil biotransformation products of azoxystrobin include Reference Compounds 2 (major, i.e., >10%), 3, 10, 20, 28 and 36 (minor, i.e., <10%). Adsorption and desorption tests indicate that azoxystrobin has low to moderate mobility in soils (adsorption coefficients K_d = 2.1–36 and K_{oc} = 300–1690).

Azoxystrobin is persistent in aerobic water – anaerobic sediment systems with a mean DT_{50} of 187–239 days. Transformation products of azoxystrobin in water–sediment systems include Reference Compounds 2 (major, i.e., >10%) and 3 (minor, i.e., <10%).

Reference Compound 2 is a major product of hydrolysis and a major transformation product of azoxystrobin in the aerobic soils, anaerobic soils and water–sediment systems tested. The solubility of this compound in water was reported by the registrant as 860 mg/L, indicating that this compound is very soluble. The transformation of Reference Compound 2 is restricted in anaerobic soils, suggesting that substantial amounts may accumulate over time. Adsorption and desorption tests indicate that Reference Compound 2 has low to very high mobility in soils (K_d = 0.55–9.2, K_{oc} = 33–770).

Reference Compound 28 is a minor product of soil and aqueous photolysis and soil biotransformation of azoxystrobin. Reference Compound 30 is a minor product of soil and aqueous photolysis of azoxystrobin. Adsorption and desorption studies indicate that these compounds have low to high mobility (K_d = 1.1–17, K_{oc} = 90–810) and moderate to very high mobility (K_d = 0.29–5.4, K_{oc} = 27–250), respectively, in soils.

Field studies in Manitoba, Saskatchewan and Alberta indicate that azoxystrobin is nonpersistent to moderately persistent (DT_{50} = 14–62 days) according to the classification scheme of Goring et al. (1975). The dissipation time 90% (DT_{90}) values for azoxystrobin were estimated as >738 days, 468 days and >757 days for Manitoba, Saskatchewan and Alberta, respectively. The very long DT_{90} values for azoxystrobin indicate that there will be substantial carryover between years, particularly for crops with multiple applications. Measurable residues of azoxystrobin and Reference Compounds 2, 28 and 30 were detected in soil samples at depths of 0–10 cm only. Concentrations of Reference Compounds 2, 28 and 30 were less than 0.05 mg/g at all sampling times. No measurable residues of Reference Compound 9 were detected in any soil sample.

5.1.2 Mobility (see Appendix VI, Table 2)

Azoxystrobin is relatively stable in the environment under normal conditions. The dissipation of azoxystrobin in the environment is primarily dependent upon biotransformation. Azoxystrobin's leaching potential was evaluated using three different methods: the leaching criteria of Cohen et al. (1984), the Groundwater Ubiquity Score (GUS) assessment method of Gustafson (1989) and with the Expert System for Pesticide Regulatory Evaluations and Simulations (EXPRES) model.

Azoxystrobin satisfies most of the leaching criteria of Cohen et al. (1984), indicating that azoxystrobin has a high potential to leach to groundwater under certain climatic and soil conditions. The GUS score for azoxystrobin (2.1) indicates that it is a borderline leacher and therefore may present a risk to groundwater under certain climatic and soil conditions (Gustafson, 1989). The results of the EXPRES screening assessment also indicate that azoxystrobin has a high potential to leach to groundwater relative to other pesticides. Azoxystrobin's leaching potential was ranked much higher than those of four pesticides known from field measurements to have leached to groundwater (atrazine, dinoseb, dicamba and picloram).

Reference Compound 2 is a major biotransformation product of azoxystrobin. As Reference Compound 2 is known to be very soluble in water (solubility = 860 mg/L), to undergo limited transformation in anaerobic soils and to have K_{oc} values indicative of low to very high mobility in soils (K_{oc} = 33–770), it is likely that this compound will leach to groundwater.

The screening methods described above do not consider characteristics specific to a site (e.g., soil texture, precipitation rates) nor do they attempt to quantify the amount of pesticide that leaches or the rate at which it leaches toward the water table. The proposed use patterns and sites of a specific pesticide, therefore, should also be taken into consideration when interpreting the results of the screening assessments. See Section 6.2.1.

5.2 Expected environmental concentrations

Concentrations of azoxystrobin in environmental compartments of concern were estimated based on calculations made using simple worst-case scenarios (Table 5.2). These concentrations were used as initial approximations for estimating the potential exposure to wildlife. It was assumed that azoxystrobin was applied at the maximum Canadian label rate for each crop and that concentrations in the various environmental compartments were obtained immediately following the last of the applications. Expected environmental concentrations (EEC) in drinking water and pond water for a runoff event were calculated for canola only.

Table 5.2 Soil and water EECs

Environmental compartment	Depth (cm)	Density	EEC
Canola: One application of 125 g a.i./ha prior to bud formation, one application of 250 g a.i./ha at early bloom stage and one application of 125 g a.i./ha at pod stage DT_{50} (soil) = 65 days (field data from Saskatchewan) DT_{50} (water) = 239 days (biotransformation in aerobic water – anaerobic soil)			
Soil	15	1.5 g/cm^3	0.17 mg a.i./kg
Water (direct overspray)	30	1.0 g/mL	0.15 mg a.i./L
Pond water (following runoff event)[a]	30	1.0 g/mL	0.063 mg a.i./L
EEC for human drinking water (large watershed)[b]	246	1.0 g/mL	0.94 mg a.i./L
EEC for human drinking water (small watershed)[c]	246	1.0 g/mL	0.047 mg a.i./L
Grapes: Maximum application rate of 250 g a.i./ha at 10–14 d intervals, maximum 6 sprays/year, maximum 2 consecutive sprays DT_{50} (soil) = 135 days (biotransformation in aerobic soil) DT_{50} (water) = 239 days (biotransformation in aerobic water – anaerobic soil)			
Soil	15	1.5 g/cm^3	0.56 mg a.i./kg
Water (direct overspray)	30	1.0 g/mL	0.45 mg a.i./L
Turfgrass: Maximum application rate of 600 g a.i./ha at 10–14 d intervals; maximum annual application rate of 5 kg a.i./ha; maximum 2 consecutive sprays DT_{50} (soil) = 135 days (biotransformation in aerobic soil) DT_{50} (water) = 239 days (biotransformation in aerobic water – anaerobic soil)			
Soil	15	1.5 g/cm^3	1.8 mg a.i./kg
Water (direct overspray)	30	1.0 g/mL	1.4 mg a.i./L

[a] EC based on 100 ha watershed, 1 ha pond (30 cm deep) and 0.5% runoff of pesticide
[b] EC based on a 4000 m^3 dugout (246 cm deep), a 100–2000 ha watershed and 0.5% runoff of pesticide
[c] EC based on a 4000 m^3 dugout (246 cm deep), a 10–100 ha watershed, exposure of the soil to 75% of the applied product and 0.5% runoff of pesticide

6.0 Effects on nontarget species

6.1 Terrestrial and aquatic species

The acute toxicity of azoxystrobin was assessed for two species of terrestrial invertebrates, one species of aquatic invertebrate, two species of fish, two species of birds and several species of aquatic and terrestrial plants (Appendix VI, Table 3). Azoxystrobin is relatively nontoxic to bees and can be used around bees with a minimum of injury. Based on the toxicity categories used by the EPA, azoxystrobin can be classified as highly toxic to aquatic invertebrates, moderately to highly toxic to fish and toxic to aquatic plants. The most sensitive aquatic species tested was the freshwater diatom *Navicula pelliculosa* (no observable effect concentration [NOEC] = 20 μg/L).

Azoxystrobin is slightly toxic to practically nontoxic to bobwhite quail and mallard ducks.

Using EPA toxicity criteria, azoxystrobin was relatively nontoxic to all of the terrestrial plant species tested. Recent reports from the EPA and the registrant, however, indicate that Macintosh and Macintosh-derived varieties of apples are extremely sensitive to azoxystrobin and may be damaged by long-range transport of spray drift from vineyards. Symptoms of phytotoxicity include necrosis, leaf drop and fruit drop. Field incidents have occurred in localised areas in Pennsylvania, Michigan and the state of Washington where both grapes and apples are grown. Certain atmospheric conditions, such as fog or temperature inversions, coupled with the use of air-blast sprayers to apply azoxystrobin on grapes have led to drift from the application site and may have caused some of these incidents. Trace amounts of azoxystrobin remaining in sprayers may also cause damage to susceptible apple varieties when the sprayers are subsequently used in orchards.

The acute toxicity of Reference Compound 2, a major soil and water–sediment biotransformation product, was assessed for one species of aquatic invertebrate, one species of fish and one species of freshwater algae. This compound was found to be practically nontoxic to aquatic invertebrates and fish. The toxicity of Reference Compound 2 was three orders of magnitude less toxic to algae (NOEC = 32 mg/L) than azoxystrobin (NOEC = 25 μg/L).

6.2 Environmental risk assessment

Azoxystrobin has been shown to be moderately to highly to toxic to aquatic organisms. Using the direct overspray EECs (Table 5.2), margins of safety for azoxystrobin for three proposed use patterns were calculated for each species tested. The results are shown in Appendix VI, Table 4. The results show that azoxystrobin presents a significant risk to small mammalian species and most aquatic organisms when used at the rates proposed for canola, grapes and turfgrass. The risks to aquatic organisms from drift can be mitigated through the use of a buffer zone. In addition to direct overspray, aquatic organisms may be affected by azoxystrobin entering aquatic systems via runoff after application to canola (Appendix VI, Tables 5, 6 and 7).

6.2.1 Leaching

Azoxystrobin has been proposed for use on three crops: canola, grapes and turfgrass. Canola is primarily grown in Alberta, Saskatchewan and Manitoba, with small amounts grown in Ontario and British Columbia. The three prairie provinces are characterised by relatively low rates of precipitation (Environment Canada 1993*a*) and relatively heavy chernozemic soils (Agriculture Canada 1977). Cropped areas tend to have clayey soils with high moisture-holding capacity (Agriculture Canada 1977). Field studies conducted with azoxystrobin over the course of two consecutive seasons in the prairie provinces showed that measurable residues of azoxystrobin and its transformation products were detected only in soil samples collected from depths of 0–10 cm. It is unlikely that the leaching of azoxystrobin and its transformation products will become an environmental concern in the prairie provinces under normal conditions.

Grapes are primarily grown in southern Ontario and British Columbia. Southern Ontario receives considerably more rainfall than the prairie provinces (Environment Canada 1993*b*). The regional PMRA office in London, Ontario, has indicated that excellent drainage is critical to the vineyard success in southern Ontario and that nearly all vineyards are equipped with extensive tile drainage systems. The proposed application rate for grapes is 200–250 g a.i./ha per application with up to six applications per year. Azoxystrobin and its transformation products, therefore, present a leaching risk to groundwater at vineyards in southern Ontario.

Grapes in British Columbia are primarily grown in the southern Okanagan Valley. Precipitation rates in the Okanagan Valley are comparable to or lower than those in the prairie provinces (Environment Canada 1993*c*), requiring growers to irrigate their crops. Grapes growing in the Okanagan Valley require 610–1220 mm irrigation, depending on the season (BCMAFF 1994). Grapes are best grown on well to rapidly drained soils (BCMAFF 1994). Accordingly, vineyard soils in the southern Okanagan Valley are coarse textured with 1–2% organic matter. The regional PMRA office in Kelowna, B.C., notes that growers in the region monitor soil moisture frequently and are conscientious about the efficient use of water on coarse soils (i.e., keeping water trapped in the root zone). The majority of vineyards in the Okanagan Valley, particularly in the southern end, are not adjacent to major waterways. Unless irrigation water is efficiently and carefully managed, azoxystrobin and its transformation products present a leaching risk to groundwater in the Okanagan Valley.

Sod grown for commercial purposes is primarily grown in Ontario and Quebec, with small amounts grown in British Columbia. Turfgrass is also maintained on golf courses across the country. In general, turfgrass on golf courses is intensively managed and watered frequently. Additionally, golf courses are constructed to drain quickly so that golfers may resume play as soon as possible following a rainfall. Azoxystrobin and its transformation products, therefore, present a leaching risk to groundwater at sites near golf courses.

6.2.2 Persistence and carryover

Laboratory studies have shown that azoxystrobin is moderately persistent in aerobic soils (DT_{50} = 54–135 days), slightly persistent in anaerobic soils (DT_{50} = 36–45 days) and persistent in aerobic water – anaerobic sediment systems ($t_{½}$ = 187–239 days). Field studies in Manitoba, Saskatchewan and Alberta indicate that azoxystrobin is nonpersistent to moderately persistent (DT_{50} = 14–65 days). The dissipation of azoxystrobin in the field is biphasic, with DT_{90} values from 468 to >757 days.

The relatively long soil biotransformation DT_{50} values for azoxystrobin indicate that there will be a substantial carryover between years, particularly for crops with multiple applications. Single applications of 500 g a.i./ha of azoxystrobin to bare soil plots in the prairies in the spring resulted in a carryover of 19.6–35.7% at the end of the first season. As the biotransformation of azoxystrobin in soil is biphasic and the estimated DT_{90} values are very long (from 468 days in Saskatchewan to >757 days in Alberta), application of

azoxystrobin in consecutive years may result in substantial accumulation of the compound in soil.

6.3 References

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7.0 Integrated efficacy summary

7.1 Grapes

7.1.1 Effectiveness against *Phomopsis* cane and leaf spot caused by *Phomopsis viticola*

The data submitted are not suitable to assess the efficacy of azoxystrobin, since the level of disease in the untreated check was too low to provide potential for control. This claim is not supported.

7.1.2 Effectiveness against downy mildew of grapes caused by *Plasmopara viticola*

Control of downy mildew was reported in six trials conducted over three years in Canada (four trials) and the U.S. (two trials).

At the proposed rates of 200 or 250 g a.i./ha, excellent control of disease symptoms (>99%) was recorded in four trials where azoxystrobin was applied as part of season-long spray programs, in alternation with registered products or in tank-mix with the commercial standard. Less consistent control of symptoms on leaves or bunch (49 –100% range) was achieved when azoxystrobin was applied alone (six or seven applications, three trials). In all trials, the level of control achieved with azoxystrobin at the recommended rates was comparable to that of the commercial standard. A rate lower than proposed (125 g a.i./ha), tested in one trial, failed to adequately control downy mildew.

The data support the claim for control of downy mildew of grapes.

7.1.3 Effectiveness against powdery mildew of grapes caused by *Uncinula necator*

Five of the submitted trials, conducted in Canada (three trials) and the U.S. (two trials) over four years, provided information that could be used for the efficacy review.

Control of disease symptoms on leaves and fruit was 94–100% (three trials) under light or moderate disease pressure and 40–100% under severe disease pressure (one submitted trial and four studies reported in literature: Muza and Travis, 1998*a*, 1998*b*; Northover and Homeyer, 1998; Wilcox and Riegel, 1997) when azoxystrobin was applied at the proposed rates (200–250 g a.i./ha) alone or as part of a season-long spray program. In all trials the performance of azoxystrobin was comparable to or better than the performance of the commercial standard.

The data support the claim for control of powdery mildew of grapes.

7.1.4 Effectiveness against black rot of grapes caused by *Guignardia bidwellii*

A level of disease high enough to provide potential for control developed in four trials conducted over three years in Canada (three trials) and the U.S. (one trial).

Control of disease incidence and severity on leaves and fruit was >91% (two trials) and 65–80% (one trial), respectively, under very light disease pressure, and >96% (three trials) under moderate disease pressure, when azoxystrobin was applied alone or as part of a season-long spray program, in alternation with registered products. In all trials, the performance of azoxystrobin was comparable to or better than the performance of the commercial standard. These data are supported by a study published in literature where, under heavy disease pressure, control of incidence and severity on fruit was 45–60% and >95%, respectively. The spray schedule that included azoxystrobin (157–180 g a.i./ha) in alternation with commercial standards gave better control than a spray program that included only commercial standards (Baudouin, 1997).

Even though rates lower than the proposed were effective in controlling symptoms of black rot in two of the above trials, the number of data points is not sufficient to guarantee consistence. Taking into account the risk of selection of resistant populations when dealing with fungicides with a very specific mode of action, such as azoxystrobin, the use of highly effective rates is essential in delaying the development of resistance in field settings.

The data support the claim for control of black rot of grapes.

7.2 Canola

7.2.1 Effectiveness against blackleg of canola caused by *Leptosphaeria maculans*

Control of blackleg of canola was reported in 14 trials conducted over four years across the prairie provinces, Ontario and North Dakota.

Application of azoxystrobin, formulated as 80WG, significantly reduced the percentage of plants with severe stem-girdling. The reduction of symptoms appeared to be rate-dependent. While considerable higher protection was achieved with 125 g a.i./ha than with 100 g a.i./ha (57 and 45% average control, respectively; $n = 7$), however, no improvement over the proposed rate (125 g a.i./ha) was achieved with the higher rate of 150 g a.i./ha (57% control; $n = 7$). Similar results were achieved with azoxystrobin formulated as 25SC. In all trials, the performance of azoxystrobin was consistently comparable or superior to the performance of the commercial standard.

The data support an application rate of 125 g a.i./ha.

Timing of application

Two strains of *Leptosphaeria maculans* infect canola: avirulent and virulent. While the avirulent strain infects the ripening crop and causes little or no yield loss, the virulent strain infects canola seedlings and progressively damages the growing crop (Evans et al., 1995). To prevent yield loss, foliar fungicides should be applied early, particularly under disease-conducive conditions. Although on the proposed label the application of azoxystrobin is recommended prior to bud formation, all submitted data are from trials conducted on plants at the 2- to 6-leaf stage of growth. No data between this early stage and bud formation (about 10–12 leaf) were submitted. Since the time of application

appears to be crucial in the control of black leg of canola, efficacy of applications at a stage of growth later than that for which data have been submitted is not supported.

The data support the claim for control of black leg of canola with applications at the 2- to 6-leaf stage of growth.

7.2.2 Effectiveness against *Sclerotinia* stem rot of canola caused by *Sclerotinia sclerotiorum*

Control of *Sclerotinia* stem rot was reported in 10 trials conducted over four years in locations across the prairie provinces.

Azoxystrobin, applied at early flowering, significantly reduced disease symptoms at the recommended rates of 175 g a.i./ha (61% control, 47–88% range, five trials) and 250 g a.i./ha (71% control, 50–94% range, nine trials). Although control was not always at optimum level, in all trials the performance of azoxystrobin was comparable to the performance of the commercial standard.

These data support the claim for control of *Sclerotinia* stem rot.

7.2.3 Effectiveness against black spot of canola caused by *Alternaria spp.*

A level of disease high enough to provide potential for control (>10% diseased pods) developed in nine trials conducted over two years in locations across the prairie provinces.

Applications of azoxystrobin at the time (30% flowering) and rate (175 g a.i./ha) proposed for the control of *Sclerotinia* stem rot are expected to suppress symptoms of black spot. However, a later application (90% flowering) is needed for disease control and prevention of yield loss. In four submitted trials, early applications of azoxystrobin at the rate recommended for the control of *Sclerotinia* stem rot, provided an average of 53% control of symptoms of black spot. These data indicate that application at the time and rate proposed for control of *Sclerotinia* stem rot will only provide suppression of black spot. The average control provided by the late application of azoxystrobin (formulated as 25SC) at the proposed rate of 125 g a.i./ha was 71% (four trials). Higher rates of azoxystrobin (175 or 250 g a.i./ha) did not significantly improve disease control.

These data support the claim for control of black spot of canola with application at the late flowering stage.

7.3 Turf

7.3.1 Efficacy against *Pythium* blight of turfgrass caused by *Pythium* spp.

The efficacy of azoxystrobin was tested on perennial ryegrass in four trials conducted over three years in the U.S. (three trials) and Ontario (one trial).

The average control for azoxystrobin at the recommended rate (6 g a.i./100 sq m) was 87% (three trials). A rate lower than proposed (3 g a.i./100 sq m) was tested in two trials, with a control achieved of 95 and 41%, respectively. More trials are needed to assess consistency in the level of control and support the use of this lower rate.

The submitted data support the claim for control of *Pythium* blight of turfgrass. Azoxystrobin should be applied preventively when environmental conditions for disease development are present (relative humidity higher than 90% for at least nine hours; daily temperature above 27.7°C and minimum temperatures of 20°C).

7.3.2 Efficacy against brown patch of turfgrass caused by *Rhizoctonia solani*

Control of brown patch was reported in two trials, conducted on tall fescue or colonial bentgrass, over two years in the U.S.

Azoxystrobin, applied at the recommended rates at intervals of 14, 21 or 28 days, provided excellent control of brown patch, regardless of the rate or the interval between applications. The overall average control was 98%. These data were supported by published work. The overall control of naturally occurring brown patch in four trials conducted on turfgrass maintained under golf course fairway conditions in the U.S. was 94%, regardless of the rate (3 or 6 g a.i./100 sq m) or the interval between treatments (one to three weeks) (Grogan and Scott, 1997; Milus and Chalkley, 1997; Soika and Tredway, 1997; Vincelli and Doney, 1997). A lower rate of azoxystrobin (1.5 g a.i./100 sq m) was tested in one of the submitted trials. Applications at 21 days interval significantly controlled brown patch on tall fescue (88% control). However, more trials are needed to assess consistency in the performance and support the use of this lower rate.

These data support the claim for control of brown patch at the rate of 3 g a.i./100 sq m.

7.3.3 Efficacy against red thread of turfgrass caused by *Laetisaria fuciformis*

One trial, conducted in the U.S. in 1993, was submitted. Under moderate disease pressure, azoxystrobin, applied at proposed rates (3–4 g a.i./100 sq m) at a two to three week interval, provided 76% control. However, more trials are needed to assess consistency in the performance of azoxystrobin in the control of red thread.

This claim is not supported.

7.3.4 Efficacy against *Fusarium* patch of turfgrass caused by *Microdochium nivale*

One trial, conducted in Ontario in 1996, was submitted in support of the control claim for *Fusarium* patch.

The average control of *Fusarium* patch with azoxystrobin applied at the recommended rates (3–6 g a.i./100 sq m) on a 14-day schedule was 92% (one trial). These data are confirmed by published work. Excellent control (95%) was reported in a trial where azoxystrobin was applied at the rate of 3 or 6 g a.i./100 sq m, on a 21- or 28-day schedule

(Soika and Tredway, 1997). In both trials, the performance of azoxystrobin was comparable to the performance of the commercial standard, regardless of the rate tested. Results obtained in trials conducted to assess the efficacy of azoxystrobin against pink snowmould (see Section 7.1.15) provide supplementary evidence of activity against *Microdochium nivale*.

These data support the claim for control of *Fusarium* patch (*Microdochium nivale*) at the rate of 3 g a.i./100 sq m.

7.3.5 Efficacy against gray snow mould (*Typhula* spp.) and pink snow mould (*Microdochium nivale*) of turfgrass

Control of gray snow mould and pink snow mould was reported in eight trials conducted over three years in Canada (three trials) and the U.S. (five trials).

In trials where gray mould was the only or the predominant disease, applications of azoxystrobin at the proposed rates (9–12 g a.i./100 sq m) effectively controlled the development of disease during the winter months (90% control, average of four trials). In one trial, a later application (December) at proposed rates was less effective (57% control, average of two rates) than earlier applications (November) at lower rates (3, 4.5 and 6 g a.i./100 sq m) (average control, 93%).

Inconsistent results were noted when azoxystrobin was applied at the proposed rate for the control of pink snow mould (two trials). Control of symptoms was 95 and 50% in plots where snow mould was the only or predominant disease, respectively. The performance of azoxystrobin, however, was comparable to the performance of the commercial standard propiconazole or a mercury product. Furthermore, in the trial where the two diseases developed at about the same rate, the overall control by azoxystrobin at the proposed rate was 87%.

Rates of azoxystrobin lower than proposed (3–6 g a.i./100 sq m) gave inconsistent results. In two trials where the disease damage was attributed solely to pink or gray snow mould, respectively, excellent control was noted (>92%). However, in a third trial where the two diseases were present at the same time, the efficacy of azoxystrobin (61%) was significantly lower than the commercial standard propiconazole at the registered rates.

These data support the claim for control of gray snow mould (*Typhula ishikariensis*) and pink snow mould (*Microdochium nivale*) on turfgrass, at 900–1200 g a.i./ha or 9–12 g a.i./100 sq m. Apply in the late fall before snow cover. Do not apply on top of snow.

7.3.6 Efficacy against necrotic ring spot of turfgrass caused by *Leptosphaeria korrae*

Three trials, conducted over two years in the U.S., were submitted in support of the control claim for necrotic ring spot on turf. In all three trials, timing of application and disease assessment are inappropriate for the disease cycle.

This claim is not supported.

7.4 Information on the occurrence or possible occurrence of the development of resistance

According to Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance Management Labelling Based on Target Site/Mode of Action*, the following statements should be incorporated on all azoxystrobin end-use products.

Group 11 Fungicide (on the primary panel)

For resistance management, please note that azoxystrobin contains a Group 11 fungicide. Any fungal population may contain individuals naturally resistant to azoxystrobin and other Group 11 fungicides. A gradual or total loss of pest control may occur over time if these fungicides are used repeatedly in the same fields. Other resistance mechanisms that are not linked to site of action but specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance-management strategies should be followed.

To delay fungicide resistance:

- Avoid application of more than two consecutive sprays of azoxystrobin or other fungicides in the same group in a season.
- Fungicide use should be based on an IPM program that includes scouting, historical information related to pesticide use and crop rotation and considers cultural, biological and other chemical control practices.
- Monitor treated fungal populations for sign of resistance development.
- If disease continues to progress after treatment with this product, do not increase the use rate. Discontinue use of this product and switch to another fungicide with a different target site of action, if available.
- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance-management and IPM recommendations for specific crops and pathogens.
- For further information and to report suspected resistance, contact (company representatives) at (toll free number) or at (Internet site).

7.5 Impact on adjacent crops

Azoxystrobin is very toxic to Macintosh apple trees and any apple varieties derived from Macintosh. Phytotoxic effects to some crabapples have also been reported. Particularly at risk are orchards close to areas where grapes are treated with azoxystrobin applied with air-blast sprayers. Droplets originated from air-blast sprayers are carried by air currents resulting in long distance transport of aerosoled azoxystrobin.

8.0 Toxic substances management policy

During the review of azoxystrobin, the PMRA has considered the implications of the federal Toxic Substances Management Policy and the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and has concluded:

Azoxystrobin meets the criteria for persistence. Its value for $t_{½}$ in aerobic water – anaerobic sediments (187–239 days) is above the TSMP Track-1 cut-off criterion for water (≥182 days).

Azoxystrobin is not likely to be bioaccumulative. Studies have shown that the octanol–water partition coefficient (log K_{ow}) is 0.39, which is below the TSMP Track-1 cut-off criterion of ≥5.0.

The toxicity of azoxystrobin is described in Sections 3.0 and 6.0.

Azoxystrobin does not contain any by-products or microcontaminants that meet the TSMP Track-1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

In the environment, azoxystrobin forms one major transformation product, Reference Compound 2. Although the transformation of this compound was found to be restricted in anaerobic soils, insufficient data were submitted to determine its $t_{½}$ in soil, water or sediments. No data were submitted on the bioaccumulation of Reference Compound 2. Reference Compound 2 has a high solubility (860 mg/L) and relatively low values of K_{oc} (33–770). Using these values, the log K_{ow} of Reference Compound 2 was calculated to be 1.4–2.8. Reference Compound 2 is unlikely to meet the criteria for bioaccumulation under the TSMP because of its high water solubility and low K_{oc}. Reference Compound 2 was practically nontoxic to aquatic invertebrates and fish.

The formulated product does not contain any formulants that are known to contain TSMP Track-1 substances.

9.0 Regulatory decision

Azoxystrobin has been granted temporary registrations for use on canola, grapes and turf, pursuant to Section 17 of the Pest Control Product Regulations, subject to the generation of the following studies:

- additional residue trials on canola and grapes;
- soil, shallow groundwater, surface runoff water and tile drainage outflow water monitoring of one representative Canadian vineyard in the Niagara region of Ontario (up to five years);

- soil and shallow groundwater monitoring of one representative Canadian vineyard in the Okanagan Valley, British Columbia (up to five years);
- soil, springtime surface runoff water and tile drainage outflow water of one representative Canadian golf course (up to five years);
- aged column leaching study; and
- toxicity data on nontarget predator and parasite insects.

List of abbreviations

ADI	allowable daily intake
a.i.	active ingredient
bw	body weight
CAS	Chemical Abstract Services
d	day
DFR	dislodgeable foliar residue
DT_{50}	dissipation time 50%
DT_{90}	dissipation time 90%
EC_{25}	effective concentration 25%
EC_{50}	median effective concentration
EEC	expected environmental concentrations
EPA	Environmental Protection Agency
♀	female
F_0	parent generation
F_1	first filial generation
F_2	second filial generation
FOB	functional observational battery
GC	gas chromatography
h	hour
ha	hectare
K_d	adsorption coefficient (ratio of concentration in the soil phase to that in the aqueous phase, under test conditions)
K_{oc}	adsorption coefficient (relates K_d to the organic carbon content of the soil sample)
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOEC	lowest observable effect concentration
LOQ	limit of quantitation
♂	male
MOE	margin of exposure
ϵ	molar absorptivity
MRL	maximum residue limit
NOAEL	no observable adverse effect level
NOEC	no observable effect concentration
NOEL	no observable effect level
NPD	nitrogen–phosphorus detection
NZW	New Zealand white
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
ROC	residue of concern
RSD	relative standard deviation
$t_{½}$	half-life

TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
TRR	total radioactive residue
λ	wavelength

Appendix I Summary of uses

Crop	Application timing	Product	Rate of application	No. of applications	Rate per season	Disease controlled
Grapes	1 week after leaves have expanded to veraison, every 10–14 days	ABOUND FlowableFungicide (250 g/L SC) ABOUND Fungicide (800 g/kg WG)	200–250 g a.i./ha	6/season maximum; alternate with other products every second application		Black rot
	From prebloom to preharvest, every 10–14 days					Downy mildew
	From prebloom to preharvest, every 10–14 days					Powdery mildew
Canola	2- to 6-leaf stage of growth	QUADRIS Flowable Fungicide (250 g/L SC) QUADRIS Fungicide (800 g/kg WG)	125 g a.i./ha	3/season maximum		Black leg
	At pod stage (90% petal fall)		125 g a.i./ha			Black spot
	Prior to 30% bloom		175–250 g a.i./ha			*Sclerotinia* stem rot
Turf	Every 10–14 days from late May to June	HERITAGE Fungicide (500 g/kg WG)	600 g a.i./ha		Do not apply more than 5 kg a.i./ha per season	*Pythium* spp.
	Every 14–28 days		300 g a.i./ha			Brown patch
	Spring or fall under prolonged wet and cool conditions every 14-28 days		300 g a.i./ha			*Fusarium* patch
	Late fall before first snow		900–1200 g a.i./ha	One		Pink and gray snow mould

Appendix II Summary of residue analysis of plants and animal products

Multi-residue methods for residue analysis
Azoxystrobin could not be quantified by accepted multi-residue methods.

Methods for residue analysis of plants and plant products
Data gathering method
NPD–GC (LOQ = 0.01 ppm for each isomer)

ROC: parent azoxystrobin plus the *Z*-isomer namely: methyl (*E*)–2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate including the isomer methyl (*Z*)–2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate

Commodity	Fortification level (ppm)	% Recovery			
		Azoxystrobin	Mean (RSD)	*Z*-isomer	Mean (RSD)
Apple	0.1–2.0	94–107 (25)	102 (4)	96–112 (25)	104 (4)
Banana, whole fruit	0.01, 0.5	78–120 (12)	102 (5)	70–115 (12)	107 (7)
Banana, pulp	0.01, 0.1	70–110 (12)	100 (3)	70–105 (12)	108 (6)
Cereal, forage	0.2, 2.0	94–99 (4)	99 (3)	93–102 (4)	102 (6)
Cereal, grain	0.05	96–104 (4)	101 (4)	88–106 (4)	96 (7)
Cereal, straw	0.1	105–108 (4)	102 (6)	98–110 (4)	96 (2)
Chili	0.01–0.20	81–114 (14)	98 (8)	101–114 (14)	103 (3)
Cucumber	0.1–0.5	97–103 (9)	100 (2)	104–111 (9)	108 (3)
Grapes	0.01–0.50	94–106 (20)	100 (5)	95–106 (20)	98 (4)
Melon, pulp	0.2–0.5	98–109 (6)	101 (7)	101–112 (4), **124–125 (2)**	111 (12)
Melon, skin	0.02–0.1	95–115 (6)	103 (4)	101–112 (4), **124–125 (2)**	105 (4)
Grapes, wine	10–500 µg/L	96–106 (20)	100 (3)	94–106 (20)	100 (3)
Leafy crop	0.05–0.20	94–110 (7)	103 (7)	92–109 (7)	102 (7)
Millet, forage	0.01	81, 112 (2)		89, 100 (2)	
Millet, grain	0.01	115 (1), **129 (1)**	—	102, 113 (2)	107
Millet, hay	0.01	**68 (1)**, 81 (1)	—	75, 100 (2)	—
Millet, straw	0.01	70, 97 (2)	—	96, 99 (2)	—
Mustard greens, leaves	0.01	**124 (2)**	—	108 (2)	—
Orange, juice	0.01–0.05	98–113 (8)	104 (5)	97–107 (8)	105 (1)
Peaches	0.1, 0.2	90–109 (30)	100 (4)	102–114 (30)	108 (3)

Commodity	Fortification level (ppm)	% Recovery			
		Azoxystrobin	Mean (RSD)	*Z*-isomer	Mean (RSD)
Pecans	0.01–0.10	96–101	98 (2)	96–112	106 (5)
Peanut, nutmeats	0.05, 0.10	94–116 (17)	100 (4)	88–104 (17)	100 (4)
Peanut, hulls	0.10–1.0	92–118 (14)	103 (2)	95–115 (14)	107 (5)
Peanut, hay	0.2–1.0	91–106 (16)	—	90–104 (16)	—
Peanut, nutmeats (processing study)	0.05	100, 102 (2)	—	88, 90 (2)	—
Peanut, hulls (processing study)	0.1–2.0	99–105 (3)		101–113 (3)	
Peanut, meal	0.05, 0.1	95–108 (4)		92–104 (4)	
Peanut, oil	0.05, 0.1 mg/L	93–106 (6)		96–107 (6)	
Radish, tops	0.01	116 (1)	—	79 (1)	—
Radish, roots	0.01	119 (1)	—	99 (1)	—
Rice, grain	0.1–1.0	98–111 (19)	102 (3)	95–108 (14)	103 (4)
Rice, straw	0.50–5.0	95–105 (13)	100 (3)	93–114 (13)	102 (6)
Root crop	0.05–0.20	98–102 (3)	101(2)	90–97 (3)	102 (7)
Tomatoes	0.05–0.2	93–107 (34)	102 (3)	90–118 (34)	113 (6)
Tomatoes (processing study)	0.05	102–104 (3)	102 (2)	106–108 (3)	106 (4)
Tomato, paste	0.1	101 (1)		111 (1)	
Tomato, pomace	0.5	99, 100 (2)		99, 102 (2)	
Turnip, tops	0.01	**128 (1)**	—	104 (1)	—
Turnip, root	0.01	111 (1)	—	118 (1)	—
Wheat, hay	0.01–10.0	75–116 (18)		82–114 (17), **125 (1)**	
Wheat, grain	0.01–0.05	81–118 (18)	97 (6)	76–119 (18)	107 (7)
Wheat, straw	0.01–2.0	93–120 (13)	99 (8)	81–115 (13)	90 (10)
Wheat, grain (processing study)	0.1	103, 108 (2)	107 (5)	93, 98 (2)	99 (3)
Wheat, bran	0.1	115 (2)		98, 99 (2)	
Wheat, millings	0.1	101 (1)		99 (1)	

Commodity	Fortification level (ppm)	% Recovery			
		Azoxystrobin	Mean (RSD)	*Z*-isomer	Mean (RSD)
Wheat, shorts	0.1	103 (1)		101 (1)	
Wheat, germ	0.1	107 (1)		99 (1)	
Wheat, flour	0.1	101 (2)		102 (1)	

Confirmatory method
LC/MS with selected ion monitoring
Recoveries were acceptable

Enforcement method
Enforcement method equivalent to data gathering method

Interlaboratory validation (ILV)
Interlaboratory validation indicated good reliability and reproducibility

Analytical method: animal matrices
Data gathering method
NPD–GC (LOQ = 0.01 ppm for each isomer)

ROC: parent azoxystrobin plus the *Z*-isomer namely: methyl (*E*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate including the isomer methyl (*Z*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate

Commodity	Fortification level (ppm)	% Recovery			
		Azoxystrobin	Mean (RSD)	*Z*-isomer	Mean (RSD)
Milk	0.001–0.02 μg/g	76–119 (17), 74 (1)	96 (11)	79–119 (18)	102 (14)
Liver	0.01–0.10 μg/g	78–1115 (17), 122 (1)	98 (12)	84–114 (17), 125 (1)	99 (10)
Muscle	0.01–0.1 μg/g	86–106 (6)	97 (7)	87–120 (5), 140 (1)	112 (20
Fat	0.01–0.10 μg/g	85–97 (5), 124 (1)	99 (13)	91–111 (6)	100 (8)
Eggs	0.01–0.10 μg/g	78–100 (16)	86 (7)	91–110 (16)	98 (6)

Confirmatory method
LC/MS with selected ion monitoring
Recoveries were acceptable

Enforcement method
Enforcement method equivalent to data gathering method

Interlaboratory validation (ILV)
Interlaboratory validation indicated good reliability and reproducibility

Appendix III Summary of toxicology studies for azoxystrobin

Toxicokinetics and metabolism: rat **Absorption and excretion**: rapid and extensive absorption and excretion following oral administration; majority within 48 h; majority excreted within 48 h; mainly in feces ((73–89%) compared with urine (9–18%); in bile cannulated rats: bile (72–74%) > feces (15%) > urine (2–7%); minor sex or dose regimen differences **Distribution**: wide distribution in all tissues by 24 and 48 h; by day 7 post-dosing, <1% in tissues and carcass **Metabolites**: 15 metabolites identified (6 unidentified); minor sex difference; main metabolite a glucuronide conjugate of the methoxyacid on the phenylacrylate moiety (29%); second major group of metabolites included hydroxylation and conjugations of the cyanophenyl moiety (conjugates of glucuronide, glutathione, cysteine, cysteinyl–glycine or mercapturate; <10% each); minor demethoxylation of phenylacrylate acid moiety and cleavage of ether linkages (<10% each)			
Acute			
Oral	Rat (Wistar) (5/sex) limit dose 5000 mg/kg bw	LD_{50} > 5000 ♂♀ no mortality; minimal clinical signs	Low toxicity
Dermal	Rat (Wistar) (5/sex) limit dose 2000 mg/kg bw	LD_{50} > 2000 ♂♀ no mortality or clinical signs, slight erythema	Low toxicity
Inhalation	Rat (Wistar) (5/sex) 0.24, 0.48, 0.72 or 0.97 (♂) mg/L air	LC_{50} = 0.96 ♂ / 0.70 ♀ (mg/L air) mortality at ≥0.48 mg/Lair; clinical signs ≥0.24 mg/L air	Slight toxicity
Skin irritation	Rabbit (New Zealand white [NZW]) (6 ♀) 500 mg; Draize	Primary irritation $score_{1-72h}$ = 0.41	Minimal dermal irritant
Eye irritation	Rabbit (NZW) (6 ♀) 100 mg; Draize	Maximum average $score_{1h}$ = 4.3	Minimal eye irritant
Skin sensitization	Guinea pig (Dunkin Hartley) Maximization test	negative	Not a sensitizer

Study	Species (strain) and dose levels	NOEL or NOAEL (mg/kg bw/day)	Observations
Short-term			
90-d dietary	Mouse (C57BL/10JfAP/Alpk) 0, 100, 1000, 3000 or 7000 ppm [♂ 0, 17, 188, 569 or 1280 mg/kg bw/day] [♀ 0, 21, 227, 675 or 1468 mg/kg bw/day] (10/sex/dose)	17	1280 ♂ / 1468 ♀ all animals sacrificed in extremis week 3 569 ♂ / 675 ♀ ↓ body weight and food utilization, ↑ relative liver weight, liver pathology 188 ♂ / 227 ♀ ↓ body weight ♀, ↓ food utilization ♂,↑ relative liver weight ♂, liver pathology ♀

Study	Species (strain) and dose levels	NOEL or NOAEL (mg/kg bw/day)	Observations
90-d dietary	Rat (Alpk:APfSD) 0, 200, 2000 or 4000 ppm [♂ 0, 20, 211 or 444 mg/kg bw/day] [♀ 0, 22, 223 or 449 mg/kg bw/day] (12/sex/dose)	20	444 ♂ / 449 ♀ ↓ body weight, ↓ food consumption and utilization, distended abdomens, altered hematology and clinical chemistry (liver), ↑ relative liver and kidney weights, bile duct and liver pathology ♂ 211 ♂ / 223 ♀ ↓ body weight, ↓ food consumption and utilization, distended abdomens, altered clinical chemistry, ↑ relative liver weight, ↑ relative kidney weight ♀
21-d dermal	Rat (Wistar) 0, 200, 500 or 1000 mg/kg bw/day (5/sex/dose)	≥1000	no treatment-related toxicity at highest dose tested
90-d capsule	Dog (beagle) 0, 10, 50 or 250 mg/kg bw/day (4/sex/dose)	10	250 ↓ body weight, clinical signs (salivation, fluid feces), altered clinical chemistry parameters (liver), ↑ liver and thyroid weights ♀ 50 ↓ body weight ♀, altered clinical chemistry ♂, ↑ liver weight ♀ 10 altered clinical chemistry ♂
1-year capsule	Dog (beagle) 0, 3, 25 or 200 mg/kg bw/day (4/sex/dose)	25	200 clinical signs (fluid feces, salivation ♀), altered clinical chemistry (liver), ↑ liver weight 25 altered clinical chemistry ♂, ↑ liver weight ♀
Chronic toxicity and oncogenicity			
2-year dietary	Mouse (C57BL/10JfAP/Alpk) 0, 50, 300 or 2000 ppm [♂ 0, 6, 38 or 272 mg/kg bw/day] [♀ 0, 9, 51 or 363 mg/kg bw/day] (55/sex/dose)	38	272 ♂ / 363 ♀ ↓ body weight, ↓ food utilization, ↑ liver weight; not oncogenic
2-year dietary	Rat (Alpk:APfSD) ♂ 0, 60, 300 or 1500 (×52 weeks) + 750 (×52 weeks) ppm [0, 4, 18 or 108–134 mg/kg bw/day] ♀ 0, 60, 300 or 1500 ppm [0, 5, 22 or 117 mg/kg bw/day] (52/sex/dose)	18	108–134 ♂ / 117 ♀ ↓ survival ♂, distended abdomens ♂, hunched ♂, ↓ body weight, ↓ food consumption and utilization, ↓ adrenal and kidney weights, bile duct and liver pathology ♂; not oncogenic

Study	Species (strain) and dose levels	NOEL or NOAEL (mg/kg bw/day)	Observations
Reproductive and developmental toxicity			
Multi-generation reproduction	Rat (Alpk:APfSD) 0, 60, 300 or 1500 ppm [♂ 0, 6, 32 or 165 mg/kg bw/day] [♀ 0, 7, 34 or 175 mg/kg bw/day] (26/sex/dose)	maternal 34 reproductive 34	165 ♂ / 175 ♀ F_0/F_1 adult ↓ body weight, ↓ food consumption, ↑ liver weight, bile duct and liver pathology ♂ F_1/F_2 pups ↓ body weight during lactation period, ↑ liver weight
Teratogenicity	Rat (Wistar) 0, 25, 100 or 300 mg/kg bw/day gd 7–16 (24/dams/dose)	maternal 25 developmental 100	maternal 300 excessive maternal toxicity (discontinued) 100 ↓ body weight, ↓ food consumption, diarrhea, urinary incontinence, salivation 25 salivation developmental 100 marginal delayed ossification; not teratogenic
Teratogenicity	Rabbit (NZW) 0, 50, 150 or 500 mg/kg bw/day gd 8–20 (21 mated/dose)	maternal 150 developmental 500	maternal 500 ↓ body weight, ↓ food consumption 150 transient ↓ food consumption developmental no significant effects; not teratogenic
Neurotoxicity			
Acute neurotoxicity	Rat (Alpk:APfSD) 0, 200, 600 or 2000 mg/kg bw	systemic 600 neurotoxicity 2000	systemic 2000 ↓ body weight ♂ (marginal) ≥200 transient diarrhea and gastric irritation neurotoxicity no effect on functional observational battery (FOB), motor activity, brain weight or neuropathology; not selectively neurotoxic
13-week neurotoxicity	Rat (Alpk:APfSD) 0, 100, 500 or 2000 ppm [♂ 0, 8, 39 or 161 mg/kg bw/day] [♀ 0, 9, 48 or 202 mg/kg bw/day]	systemic 39 neurotoxicity 161	systemic 161 ♂ / 202 ♀ ↓ body weight ♂, ↓ food consumption and utilization ♂ neurotoxicity no effect on FOB, motor activity, brain dimensions or neuropathology; not selectively neurotoxic

Mutagenicity	
Bacterial cell gene mutation assay (in vitro) *S. typhimurium* (TA1535, TA1537, TA98, TA100) *E. coli* (WP2P, WP2P uvrA)	negative (±S9)
Mammalian cell gene mutation assay (in vitro) L5178Y mouse lymphoma cells	positive (±S9)
Mammalian cell cytogenetics assay (in vitro) Human lymphocytes	positive (±S9)
Mammalian cell cytogenetics study (in vivo) Mouse bone marrow micronucleus	negative
DNA damage and repair study (unscheduled DNA synthesis) (in vivo) Rat hepatocytes (male)	negative

Appendix IV Summary of residue studies

Plant metabolism
Information illustrating the plant metabolism in grape, peanut and wheat was submitted. Based on the results of these plant metabolism studies, the Food Residue Exposure Assessment Section (FREAS) can conclude that the metabolism of azoxystrobin in the three different crops is qualitatively and quantitatively similar. **Under these conditions, FREAS believes the nature of the residue in plants to be understood.**
ROC: parent azoxystrobin and the *Z*-isomer

Matrix	Preharvest interval [PHI] (days)	^{14}C-cyanophenol total radioactive residue [TRR] (ppm)	^{14}C-pyrimidinyl TRR (ppm)	^{14}C-phenylacrylate TRR (ppm)
Grapes (fruit)	21	0.371	1.35	0.965
Peanuts (nutmeat)	144	0.24	0.60–0.65	0.47–0.49
Wheat (grain)	62	0.066–0.075	0.075–0.08	0.075–0.076

Confined crop rotation studies
2.0 kg a.i./ha (2.2× gap) soil application

Crop	Crop fraction	^{14}C-Azoxystrobin equivalent residues (ppm)
		Planting interval (30 days after treatment)
Wheat	Forage	1.18
	Straw	5.92
	Grain	0.16
Radish	Foliage	0.49
	Roots	0.12
Leaf lettuce	Foliage	0.15

Freezer storage stability tests
Stability of azoxystrobin and the *Z*-isomer at –20°C in various matrices is illustrated below.
Plant metabolism and residue samples were stored within the time periods studied.

Crop matrix (fortification level)	Storage period (months)	Azoxystrobin		*Z*-isomer	
		ppm	% recovered	ppm	% recovered
Apples (0.2 ppm)	0	0.20, 0.21	—	0.21, 0.22	—
	5	0.18, 0.18	90, 90	0.19, 0.20	95, 100
	12	0.19, 0.19	95, 95	0.21, 0.21	105, 105
	24	0.19, 0.20	95, 100	0.20, 0.20	100, 100
Bananas (0.10 ppm)	0	0.11, 0.10	—	0.11, 0.10	—
	3	0.10, 0.10	100, 100	0.10, 0.11	100, 110
	12	0.10, 0.09	100, 90	0.10, 0.08	100, 80
	24	0.09, 0.09	90, 90	0.09, 0.09	90, 90

Crop matrix (fortification level)	Storage period (months)	Azoxystrobin		Z-isomer	
		ppm	% recovered	ppm	% recovered
Cucumbers (0.10 ppm)	0	0.09, 0.09	—	0.10, 0.10	100, 100
	3	0.09, 0.10	90, 100	0.10, 0.10	100, 100
	12	0.09, 0.09	90, 90	0.10, 0.10	100, 100
	24	0.09, 0.10	90, 100	0.10, 0.10	100, 100
Grapes (0.4 ppm)	0	0.38, 0.39	—	0.40, 0.41	—
	5	0.42, 0.43	105, 108	0.39, 0.41	98, 103
	10	0.36, 0.37	90, 93	0.39, 0.40	98, 100
	14	0.38, 0.44	95, 100	0.38, 0.43	95, 108
	24	0.40, 0.39	100, 98	0.40, 0.38	100, 95
Grape, wine (100 µg/L)	0	98, 99 µg/L	—	98, 99 µg/L	—
	5	110, 112 µg/L	110, 112	110, 112 µg/L	96, 101
	10	97, 101 µg/L	97, 101	97, 101 µg/L	96, 102
	14	103, 105 µg/L	103, 105	103, 105 µg/L	102, 107
	24	100, 99 µg/L	100, 99	102, 102 µg/L	102, 102
Peaches (0.2 ppm)	0	0.21, 0.21	—	0.21, 0.22	—
	5	0.18, 0.19	90, 95	0.20, 0.20	100, 100
	12	0.19, 0.19	95, 95	0.22, 0.22	110, 110
	24	0.20, 0.20	100, 100	0.19, 0.20	95, 100
Peanuts (0.1 ppm)	0	0.10, 0.11	—	0.10, 0.11	—
	5	0.09, 0.12	90, 120	0.09, 0.09	90, 90
	12	0.08, 0.09	80, 90	0.09, 0.09	90, 90
	24	0.08, 0.08	80, 80	0.10, 0.10	100, 100
Peanut oil (100 µg/L)	0	95, 96 µg/L	—	95, 101 µg/L	—
	4	85, 97 µg/L	85, 87	84, 87 µg/L	84, 87
Peanut meal (0.1 ppm)	0	0.10, 0.10	—	0.10, 0.10	—
	4	0.09, 0.09	90, 90	0.09, 0.09	90, 90
Pecans (0.1 ppm)	0	0.09, 0.10	—	0.10, 0.10	—
	5	0.09, 0.12	90, 120	0.10, 0.10	100, 100
	12	0.08, 0.08	80, 80	0.09, 0.09	90, 90
	24	0.08, 0.08	80, 80	0.10, 0.10	100, 100
Rape (seed oil) (0.1 ppm)	0	0.09, 0.10	—	0.11, 0.11	—
	6	0.09, 0.09	90, 90	0.09, 0.09	90, 90
	12	0.10, 0.10	100, 100	0.10, 0.10	100, 100

Crop matrix (fortification level)	Storage period (months)	Azoxystrobin		*Z*-isomer	
		ppm	% recovered	ppm	% recovered
	24	0.10, 0.10	100, 100	0.10, 0.10	100, 100
Tomatoes (0.1 ppm)	0	0.10, 0.10	—	0.10, 0.11	—
	5	0.08, 0.09	80, 90	0.10, 0.11	100, 110
	12	0.09, 0.09	90, 90	0.11, 0.11	110, 110
	24	0.08, 0.08	80, 80	0.10, 0.10	100, 100
Tomato juice (0.1 ppm)	0	0.10, 0.10	—	0.11, 0.11	—
	4	0.10, 0.10	100, 100	0.10, 0.10	100, 100
Tomato paste (0.1 ppm)	0	0.10, 0.10	—	0.11, 0.11	—
	4	0.09, 0.09	90, 90	0.10, 0.11	100, 110
Wheat grain (0.10 ppm)	0	0.10, 0.10	—	0.10, 0.10	—
	5	0.12, 0.11	120, 110	0.10, 0.10	100, 100
	12	0.10, 0.10, 0.09, 0.09	100, 100, 90, 90	0.09, 0.09, 0.08, 0.08	90, 90, 80, 80
	24	0.08, 0.08	80, 80	0.08, 0.08	80, 80
Wheat straw (weathered)	0	2.3, 2.5	—	0.20, 0.21	—
	5	3.4, 3.6	142, 150	0.241, 0.29	115, 138
	10	2.7, 2.8	113, 117	0.23, 0.23	110, 110
	14	2.9, 3.1	121, 127	0.25, 0.27	119, 129
	24	2.7, 2.7	113, 113	0.24, 0.23	115, 110
Wheat bran (0.1 ppm)	0	0.10, 0.10	—	0.10, 0.10	—
	4	0.09, 0.09	90, 90	0.09, 0.09	90, 90

Animal metabolism

In the goat metabolism study, azoxystrobin was extensively metabolised. Excretion was rapid and occurred mostly through urine, but also in feces.

Poultry metabolism studies indicated that most of the dose was excreted.

ROC: parent azoxystrobin and the *Z*-isomer

Matrix	% of administered dose (ppm)
Tissues	5–20% (0.954–1.44)
Milk	<0.1% (0.004–0.011)
Feces	62.1–72.2%
Urine	18.0–23.5%

Cattle feeding study
The maximum theoretical dietary burden of azoxystrobin to beef and dairy cattle to be 4.83 and 8.96 ppm, *respectively. Based on these* dietary burdens, the dosing levels of 5, 25, 75 and 250 ppm represent 1×, 4.8×, 15× and 48× the maximum theoretical dietary burden to beef cattle and 0.6×, 2.8×, 8.4× and 28× the maximum theoretical dietary burden to dairy cattle, respectively.

The data indicate that tolerances for residues of azoxystrobin are required for milk, fat, meat, and the meat byproducts; of cattle, goats, hogs, horses, and sheep. Detectable residues of azoxystrobin were observed in the milk (<0.001–0.006 ppm) and liver (<0.01–0.01 ppm) of cattle fed azoxystrobin at ~2.8× the maximum theoretical dietary burden (lowest dosing level over 1×) for 28–30 days.

The available data support the proposed MRL for milk (0.006 ppm), and for meat and meat byproducts (0.01 ppm).

Hen feeding study
No data was submitted to illustrate the magnitude of residues in hen. Canola can be fed to chickens (15% of the diet). Exposure resulting from a diet on canola would be less ~0.05 ppm. The laying hen metabolism study reviewed above indicated that hen fed a diet of 10 ppm for 10 days had residues in edible tissues that were less than 0.1 ppm. FREAS can support this petition even though the lack of feeding data in poultry is considered a data gap. FREAS will recommend that no further expansion of use into commodities that can potentially be fed to poultry be considered.

Number of field trials by region

For grapes

Zones	1	0.042	4	5	0.2083	5B	7	9	10	11	12	14	Total
Required				4						1			5
Submitted	2 U.S.		1 U.S.	2		1 U.S.			8 U.S.	2 U.S.	1 U.S.		2* 15 U.S.**

* One growing season
** Two growing seasons
In addition, results from trials carried out in Europe were submitted.

For canola

Zones	1	0.042	3	5	0.2083	5B	6	7	10	11	12	14	Total
Required				1				1				14	16
Submitted				5				6				7	18* + 2 FRANCE

* Trials were carried out over a total of three growing seasons; two trials carried out in France were also submitted.

Supervised residue trials on canola*						
Commodity and portion analysed	**Formulation**	**Application**			**PHI (days)**	**Residues (ppm)****
		No.	**Total rate (kg a.i./ha)**	**% gap**		
Canadian trials						
Canola seed	granular	3	0.952	1.9×	23–31	0.03–0.80
* Only the data representative of the maximum gap is summarised here. ** Sum of azoxystrobin and the *Z*-isomer						
In addition to setting MRLs on grapes and canola, the PMRA has recommended MRLs on bananas, peaches, tomato and tomato paste, peanuts and pecans to cover potential residues of azoxystrobin and the *Z*-isomer in imported crops.						

Processing studies demonstrated that residues of azoxystrobin and the *Z*-isomer did not concentrate in processed grape fractions and wine. Studies carried out with canola also indicate that residues of azoxystrobin and the *Z*-isomer do not concentrate in canola oil.							
Chronic dietary risk assessment using Dietary Exposure Evaluation Model (DEEM) Software based on the 1994–1996 Continuing Survey of Food Intake by Individuals, ADI = 0.18 mg/kg bw, Tier I using the proposed MRLs and 10% allocation to water							
	Total population	**All infants (<1 year)**	**Children (1–6 years)**	**Children (7–12 years)**	**Children (13–19 years)**	**20+ years**	**Seniors 55+**
% of ADI	10.8	11.3	12.7	11	10.7	10.6	10.7

Commodity	Proposed Canadian MRLs[a] (ppm)	U.S. tolerances (ppm)[b]
Grapes	3	1
Canola	1	1
Banana	1	1
Peaches	0.8	0.8
Tomato paste	0.6	0.6
Liver	0.3	0.3
Tomato	0.2	0.2
Kidney	0.06	0.06
Peanut oil	0.03	0.03
Peanuts	0.01	0.01
Meat and meat by-products	0.01	0.01
Pecans	0.01	0.01

[a] MRLs based on data available at the time of review
[b] Based on information available at the time of review

Appendix V Summary of occupational exposure

Summary of exposure estimates and resulting margins of exposure for mixers–loaders–applicators

Product	Use	Person exposed	Total exposure[a] (unabsorbed) (μg a.i./kg bw/day)	MOE (based on a NOEL of 1000 mg/kg from a 21-day dermal rat study
QUADRIS Flowable	Canola, groundboom	Mixer–loader–applicator: farmer	54.01	18 500
		Mixer–loader–applicator: custom	147.94	6 750
	Canola, aerial	Mixer–loader	138.43	7 225
		Applicator	15.43	64 800
ABOUND flowable	Grapes, airblast	Mixer–loader–applicator:	49.95	20 000
QUADRIS Fungicide	Canola, groundboom	Mixer–loader–applicator: farmer	82.18	12 200
		Mixer–loader–applicator: custom	225.11	4 440
	Canola, aerial	Mixer–loader	236.43	4 230
		Applicator	15.43	64 800
ABOUND Fungicide	Grapes, airblast	Mixer–loader–applicator	53.63	18 650
HERITAGE Fungicide	Turf, groundboom	Mixer–loader–applicator	27.44	36 450

[a] The exposure estimates assume a body weight of 70 kg and that in a typical day 115 ha of canola will be treated by farmers, 315 ha of canola will be treated by custom applicators, 400 ha of canola will be treated aerially, 15 ha of grapes will be treated and 8 ha of turf will be treated, all at the maximum application rate specified on the label.

Summary of dermal exposure and margins of exposure for grape re-entry intervals

Time	DFR (μg/cm²)	Dermal exposure (μg/kg bw/day)	MOE
After the 3rd application as soon as spray dried	0.39	670	1490
After the 4th application as soon as spray dried	0.31	530	1885
After the 6th application			
As soon as spray dried	0.60	1000	1000
3 days post-application	0.53	920	1085
7 days post-application	0.46	780	1280
14 days post-application	0.34	590	1695
21 days post-application	0.26	450	2220

Appendix VI Summary tables of environmental studies

Table 1 Summary of transformation of azoxystrobin

Process	Value	Interpretation
Abiotic		
Hydrolysis (25°C)	pH 5, 7 stable pH 9 $t_{½}$ = 267 d	Hydrolysis is not a major route of transformation at environmentally relevant pHs and temperatures.
Phototransformation in soil (25°C)	DT_{50} = 7.7–14 d	Photolysis is a route of transformation in soil.
Phototransformation in water (25°C)	DT_{50} = 10.7–16.2 d	Direct photolysis is not expected to be a major transformation pathway in aqueous environments.
Phototransformation in river water (25°C)	DT_{50} = 5.2 d	Azoxystrobin may be subject to indirect photolysis in aqueous environments.
Biotic		
Biotransformation in aerobic soil (20°C)	DT_{50} = 54–135 d	Moderately persistent
Biotransformation in anaerobic soil (20°C)	DT_{50} = 36–45 d	Slightly persistent
Biotransformation in aerobic water – anaerobic sediment systems (20°C)	$t_{½}$ = 187–239 d	Persistent

Table 2 Summary of laboratory mobility studies[a]

Soil	Azoxystrobin	Reference Compound 2	Reference Compound 28	Reference Compound 30
Sand (Lilly Field, U.K.)	K_{oc} = 710 Low mobility	K_{oc} = 770 Low mobility	—	—
Loamy sand (Kenny Hill, U.K.)	K_{oc} = 300 Moderate mobility	K_{oc} = 34 Very high mobility	K_{oc} = 120 High mobility	K_{oc} = 27 Very high mobility
Loamy sand (East Anglia, U.K.)	K_{oc} = 360 Moderate mobility	K_{oc} = 33 Very high mobility	—	—
Loamy sand (ERTC, U.S.)	K_{oc} = 1490 Low mobility	—	K_{oc} = 380 Moderate mobility	K_{oc} = 100 High mobility
Sandy clay loam (Hyde Farm, U.K.)	K_{oc} = 700 Low mobility	K_{oc} = 65 High mobility	K_{oc} = 170 Moderate mobility	K_{oc} = 40 Very high mobility
Silty clay loam (Nebo, U.K.)	K_{oc} = 760 Low mobility	K_{oc} = 560 Low mobility	—	—
Silty clay loam (NRTC, U.S.)	K_{oc} = 1,690 Low mobility	—	K_{oc} = 810 Low mobility	K_{oc} = 250 Moderate mobility
Silty clay loam (Wisborough Green, U.K.)	—	—	K_{oc} = 90 High mobility	K_{oc} = 99 High mobility
Clay loam (Pickett Piece, U.K.)	K_{oc} = 720 Low mobility	K_{oc} = 510 Low mobility	K_{oc} = 140 High mobility	K_{oc} = 120 High mobility

[a] Mobility classifications based on McCall et al. (1981)

Table 3 Summary of environmental toxicology of azoxystrobin and its transformation products

Species	Study type	Results and interpretation
Azoxystrobin		
Earthworms (*Eisenia foetida*)	Soil contact	14-d LC_{50} = 283 mg a.i./kg soil (nominal) 14-d NOEC = 180 mg a.i./kg soil (nominal)
Honey bees (*Apis mellifera*)	Acute contact Acute oral	48-h LD_{50} > 200 μg a.i./bee (nominal) 48-h LD_{50} > 25 μg a.i./bee (nominal) relatively nontoxic
Freshwater flea (*Daphnia magna*)	Acute toxicity	48-h EC_{50} = 280 μg a.i./L (analytical) 48-h NOEC = 126 μg a.i./L (analytical) highly toxic
Freshwater flea (*Daphnia magna*)	Chronic toxicity	21-d LC_{50} = 150 μg a.i./L (analytical) 21-d NOEC = 44 μg a.i./L (analytical)
Rainbow trout (*Onchorynchus mykiss*)	Acute toxicity	96-h LC_{50} = 0.47 mg a.i./L (analytical) 96-h NOEC = 0.068 mg a.i./L (analytical) highly toxic
Bluegill sunfish (*Lepomis macrochirus*)	Acute toxicity	96-h LC_{50} = 1.1 mg a.i./L (analytical) 96-h NOEC = 0.50 mg a.i./L (analytical) moderately toxic
Fathead minnow (*Pimephales promelas*)	Early life cycle toxicity	28-d LOEC = 193 μg a.i./L (analytical) 28-d NOEC = 147 μg a.i./L (analytical)
Bobwhite quail (*Colinus virginianus*)	Single dose oral toxicity	LD_{50} > 2130 mg/kg bw (analytical) NOEC = 2130 mg/kg bw (analytical) practically nontoxic
Bobwhite quail (*Colinus virginianus*)	5-d dietary toxicity	LC_{50} > 5290 mg/kg feed (analytical) NOEC = 5290 mg/kg feed (analytical) practically nontoxic
Mallard duck (*Anas platyrhynchos*)	5-d dietary toxicity	LC_{50} > 5290 mg/kg feed (analytical) NOEC = 2550 mg/kg feed (analytical) practically nontoxic
Mallard duck (*Anas platyrhynchos*)	Reproduction	NOEC = 1200 mg/kg feed (nominal) LOEC = 3000 mg/kg feed (nominal)
Mouse	90-d dietary toxicity	NOEC = 100 mg/kg feed
Rat	90-d dietary toxicity	NOEC = 200 mg/kg feed
Mouse	2-year dietary toxicity	NOEC = 300 mg/kg feed
Rat	2-y dietary toxicity	NOEC = 300 mg/kg feed
Rat	Multi-generation reproduction	NOEC = 300 mg/kg feed
Freshwater diatom (*Navicula pelliculosa*)	Biomass curve area Growth rate	E_bC_{50} = 57 μg/L (nominal) E_rC_{50} > 320 μg/L (nominal) NOEC = 20 μg/L (nominal)
Blue-green algae (*Anabaena flos-aquae*)	Biomass curve area, growth rate	NOEC = 8.5 mg/L (analytical)

Species	Study type	Results and interpretation
Green algae (*Selenastrum capricornutum*)	Biomass curve area Growth rate	E_bC_{50} = 120 µg/L (nominal) E_rC_{50} = 1400 µg/L (nominal) NOEC = 25 µg/L (nominal)
Duckweed (*Lemna gibba*)	Frond growth Dry weight	14-d EC_{50} = 3.2 mg/L (nominal) NOEC = 0.8 mg/L (nominal) 14-d EC_{50} > 6.4 mg/L (nominal) NOEC = 3.2 mg/L (nominal)
Carrot (*Daucus carota*)	Seedling emergence Dry weight	EC_{25}, EC_{50} > 2240 g product/ha (1120 g a.i./ha)[a] NOEC = 2240 g product/ha (1120 g a.i./ha)[a] EC_{25}, EC_{50} > 1120 g product/ha (560 g a.i./ha)[a] NOEC = 1120 g product/ha (560 g a.i./ha)[a]
Reference Compound 2		
Freshwater flea (*Daphnia magna*)	Acute toxicity	48-h EC_{50} > 180 mg/L (nominal) 48-h NOEC = 32 mg/L (nominal) practically nontoxic
Rainbow trout (*Onchorynchus mykiss*)	Acute toxicity	96-h LC_{50} > 150 mg/L (analytical) 96-h NOEC = 150 mg/L (analytical)
Green algae (*Selenastrum capricornutum*)	Biomass curve area Growth rate	E_bC_{50} = 47 mg/L (analytical) E_rC_{50} = 80 mg/L (analytical) NOEC = 32 mg/L (analytical)

[a] Product = HERITAGE Fungicide 50WG formulation: all values reported as nominal concentrations

Table 4 Direct overspray margins of safety for azoxystrobin and reference compound 2 (aquatic calculations based on NOECs)

Species	Margin of safety		
	Canola	Grapes	Turf
Azoxystrobin: Acute toxicity end points			
Earthworm	1100	320	100
Bees	>56	>19	>5.6
Daphnia magna	**0.82**	**0.28**	**0.088**
Rainbow trout	**0.44**	**0.15**	**0.048**
Bluegill sunfish	3.2	1.1	**0.35**
Bobwhite quail	88	29	8.8
Mallard duck	150	50	15
Navicula pelliculosa	**0.13**	**0.044**	**0.014**
Anabaena flos-aquae	55	19	6
Selenastrum capricornutum	**0.16**	**0.055**	**0.018**
Lemna gibba	5.2	1.8	**0.56**
Carrot	>1.5	**>0.44**	**>0.14**
Mice	**0.4**	**0.13**	**0.04**
Rats	**0.79**	**0.26**	**0.079**
Azoxystrobin: Chronic toxicity end points			
Daphnia magna	**0.29**	**0.097**	**0.031**
Fathead minnow	**0.96**	**0.32**	**0.1**
Mallard duck	71	24	7.1
Reference Compound 2: Acute toxicity end points			
Daphnia magna	210	73	23
Rainbow trout	1000	340	110
Selenastrum capricornutum	210	73	23

Table 5 Pond water (following a runoff event) margins of safety for azoxystrobin following application on canola

Species	End point	EEC	Margin of safety
Azoxystrobin: Acute toxicity end points			
Daphnia magna	NOEC = 0.126 mg a.i./L	0.074 mg a.i./L[a]	1.7
Rainbow trout	NOEC = 0.068 mg a.i./L	0.074 mg a.i./L[a]	**0.92**
Bluegill sunfish	NOEC = 0.5 mg a.i./L	0.074 mg a.i./L[a]	6.7
Navicula pelliculosa	NOEC = 0.020 mg a.i./L	0.074 mg a.i./L[a]	**0.27**
Anabaena flos-aquae	NOEC = 8.5 mg a.i./L	0.074 mg a.i./L[a]	120
Selenastrum capricornutum	NOEC = 0.025 mg a.i./L	0.074 mg a.i./L[a]	**0.34**
Lemna gibba	NOEC = 0.8 mg a.i./L	0.074 mg a.i./L[a]	11
Azoxystrobin: Chronic toxicity end points			
Daphnia magna	NOEC = 0.044 mg a.i./L	0.060 mg a.i./L[b]	**0.73**
Fathead minnow	NOEC = 0.147 mg a.i./L	0.060 mg a.i./L[b]	2.4

[a] Peak EEC as calculated using GENEEC assuming a 1 ha × 30 cm pond
[b] Average 56-day EEC as calculated by GENEEC assuming a 1 ha × 30 cm pond

Table 6 Pond water (following a runoff event) margins of safety for azoxystrobin following application on grapes

Species	End point	EEC	Margin of safety
Azoxystrobin: Acute toxicity end points			
Daphnia magna	NOEC = 0.126 mg a.i./L	0.22 mg a.i./L[a]	**0.57**
Rainbow trout	NOEC = 0.068 mg a.i./L	0.22 mg a.i./L[a]	**0.31**
Bluegill sunfish	NOEC = 0.5 mg a.i./L	0.22 mg a.i./L[a]	2.3
Navicula pelliculosa	NOEC = 0.020 mg a.i./L	0.22 mg a.i./L[a]	**0.09**
Anabaena flos-aquae	NOEC = 8.5 mg a.i./L	0.22 mg a.i./L[a]	38
Selenastrum capricornutum	NOEC = 0.025 mg a.i./L	0.22 mg a.i./L[a]	**0.11**
Lemna gibba	NOEC = 0.8 mg a.i./L	0.22 mg a.i./L[a]	3.6
Azoxystrobin: Chronic toxicity end points			
Daphnia magna	NOEC = 0.044 mg a.i./L	0.18 mg a.i./L[b]	**0.25**
Fathead minnow	NOEC = 0.147 mg a.i./L	0.18 mg a.i./L[b]	**0.83**

[a] Peak EEC as calculated using GENEEC assuming a 1 ha × 30 cm pond
[b] Average 56-day EEC as calculated by GENEEC assuming a 1 ha × 30 cm pond

Table 7 Pond water (following a runoff event) margins of safety for azoxystrobin following application on turf

Species	End point	EEC	Margin of safety
Azoxystrobin: Acute toxicity end points			
Daphnia magna	NOEC = 0.126 mg a.i./L	0.075 mg a.i./L[a]	1.7
Rainbow trout	NOEC = 0.068 mg a.i./L	0.075 mg a.i./L[a]	**0.9**
Bluegill sunfish	NOEC = 0.5 mg a.i./L	0.075 mg a.i./L[a]	6.6
Navicula pelliculosa	NOEC = 0.020 mg a.i./L	0.075 mg a.i./L[a]	**0.27**
Anabaena flos-aquae	NOEC = 8.5 mg a.i./L	0.075 mg a.i./L[a]	110
Selenastrum capricornutum	NOEC = 0.025 mg a.i./L	0.075 mg a.i./L[a]	**0.33**
Lemna gibba	NOEC = 0.8 mg a.i./L	0.075 mg a.i./L[a]	11
Azoxystrobin: Chronic toxicity end points			
Daphnia magna	NOEC = 0.044 mg a.i./L	0.061 mg a.i./L[b]	**0.72**
Fathead minnow	NOEC = 0.147 mg a.i./L	0.061 mg a.i./L[b]	2.4

[a] Peak EEC as calculated using GENEEC assuming a 1 ha × 30 cm pond and a 1.1 ha watershed

[b] Average 56-day EEC as calculated by GENEEC assuming a 1 ha × 30 cm pond and a 1.1 ha watershed